CBER Update 2006

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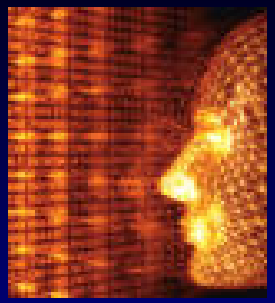
FDLI 49th Annual Conference
Washington, D.C.
April 7, 2006

Topics for today

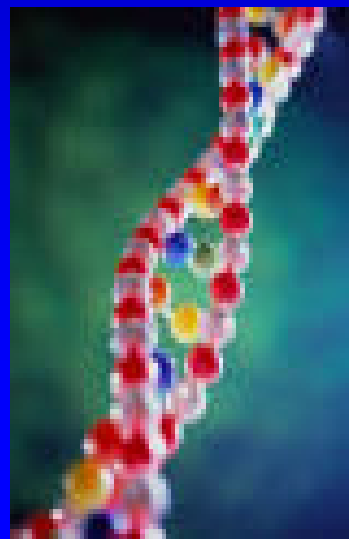
- CBER vision, mission, selected public health accomplishments
- Brief review of performance stats and related updates
- Recent CBER initiatives



Vision for CBER

INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

- **Protect and improve public and individual health in the US and, where feasible, globally**
- **Facilitate the development, approval and access to safe and effective products and promising new technologies**
- **Strengthen CBER as a preeminent regulatory organization for biologics**



Mission: Complex Products Critical for Public Health, National Preparedness & 21st Century Medicine

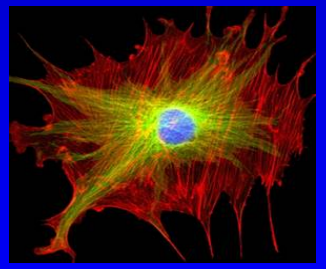
Blood Derivatives

Vaccines

Whole Blood

Blood Components

Somatic Cell & Gene Therapy



Devices

Allergenic Extracts

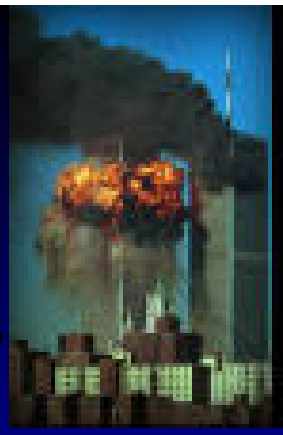
Xenotransplantation

Tissues

CBER Products Touch Many Lives and Are Essential to Current and Future Health Care

- > 235 million vaccinations each year to prevent serious infectious disease
- ~ 30 million blood & blood component transfusions
- > 1 million tissues transplanted last year to repair, restore function and improve the quality of life

Not Business as Usual



- Since 9/11, CBER has adapted to challenging circumstances through extraordinary efforts and proactive measures
  - Meetings to encourage/speed development of new products
  - Early and intensive ongoing interactions w/sponsors
  - Collaboration and rapid turnaround in product review
  - Inspections of manufacturing facilities
  - Participation in multiple product development teams
  - Critical Path Research: Targeted to more efficient, rapid product development and availability
  - Increased communication with international regulatory counterparts
- Such approaches used in West Nile response and in 2004 flu season and inform all our current activities (e.g., pandemic preparedness)

Recent Public Health Accomplishments

- New Products to Patients
- Guidance for Industry and FDA review staff
- Rulemaking

Important New CBER Products to Patients

- First combination whooping cough vaccines for adolescents/adults (Adacel, Boostrix)
- New meningococcal conjugate vaccine (Menactra)
- New influenza vaccine, accelerated approval (Fluarix)
- New rotavirus vaccine (Rotateq)
- HepaGamB (Hepatitis B immune globulin)
- Vaccinia Immune globulins (IV)
- HIV Rapid Test – oral fluid
- New blood screening tests for HIV, hepatitis B, and West Nile virus
- New blood compatibility testing options

Guidance Documents

- CY 2005 to present
  - CBER issued 14 guidance documents (10 draft, 4 final)
  - CBER participated in the development of >45 draft and final guidance documents with other agency components

Recent CBER Guidance: Examples

- Vaccine development (new in 2006)
  - Clinical data for licensure of influenza vaccines (pandemic and annual)
  - Developmental toxicology recommendations for vaccines against infectious diseases
- IVIG as replacement therapy for PID: Recommendations for safety, efficacy, and PK
- NAT testing for HIV and HCV: Testing, product disposition, donor deferral, and reentry
- Adverse event reporting for gene therapy trials

Recent Agency Guidance: Examples

- Establishment and operation of clinical trial data monitoring committees (final)
- Formal Dispute Resolution: Scientific and technical issues related to pharmaceutical cGMP (final)
- Fast Track Drug Development Programs – Designation, development and application review (final)
- Product Labeling: implementing new content and format requirements (final)
- Approaches to complying with cGMP during Phase 1 (draft)
- Emergency use authorization of medical products (draft)
- Clinical trial endpoints for the approval of cancer drugs and biologics (draft)

CBER Rulemaking CY2005 to present

- **8 proposed and final rules issued by CBER and published in the Federal Register, including:**
  - **Human cells, tissue, and cellular and tissue-based products: Donor screening and testing, and related labeling, interim final rule**
  - **Medical devices: Hematology and Pathology Devices: Reclassification from Class III to Class II of automated blood cell separator device operating by centrifugal separation principle, proposed rule.**
  - **Biological Products: Bacterial Vaccines and Toxoids: Implementation of Efficacy Review; Final Rule and Final Order**

Agency Rulemaking CY 2005 to present

- CBER participated in clearance of 4 additional final rules and 1 proposed rule, for which other agency components had the lead
  - Definition of primary mode of action (final)
  - Content and format of labeling for human prescription drugs and biologics (final)
  - Export requirements for unapproved new drug products (final)
  - Current GMP regulation and investigational new drugs (direct final), with companion proposed rule

CBER Regulatory Activities
A few interesting numbers…

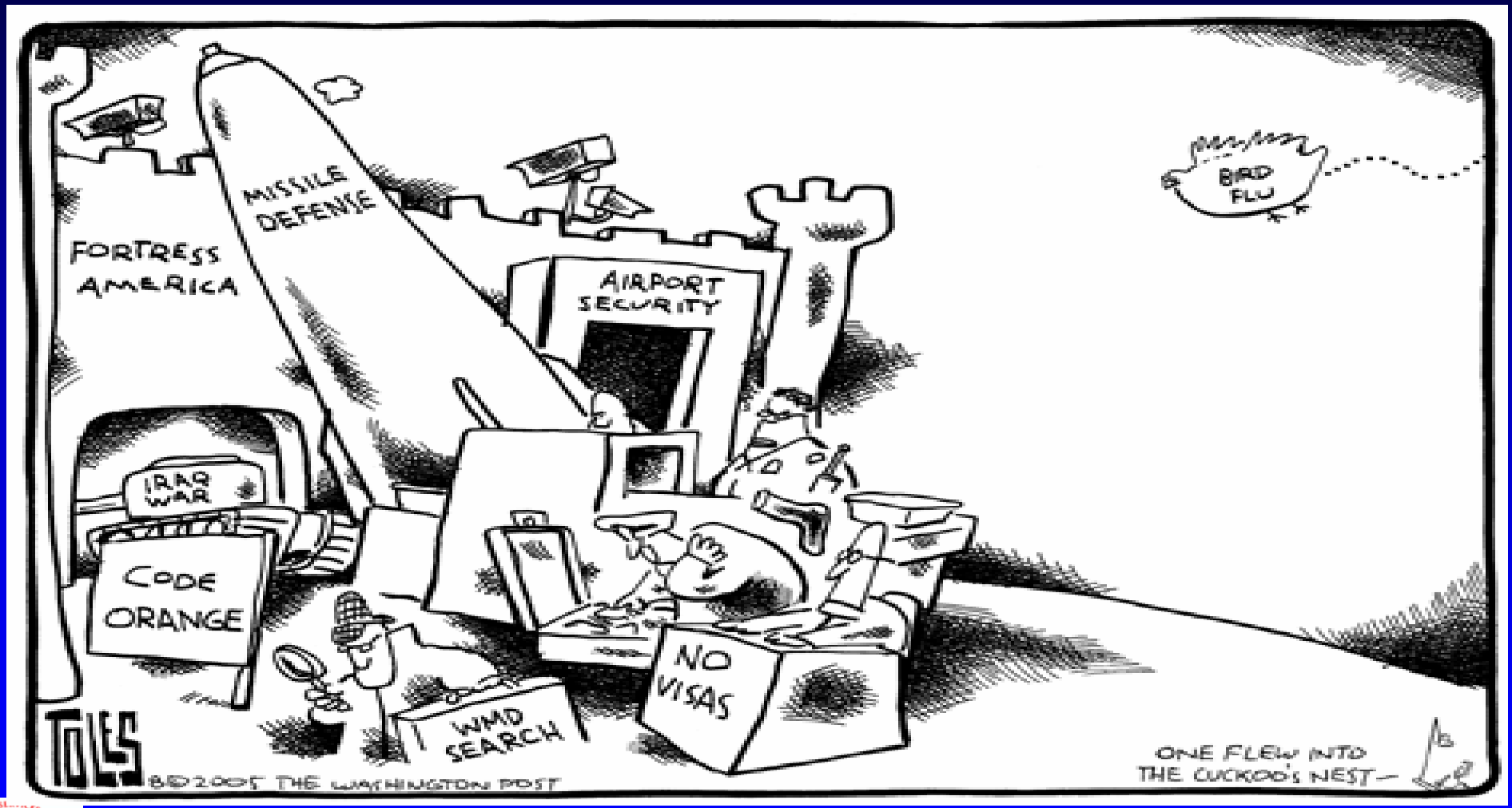
- ~ 1000 active clinical studies of cell, gene, tissue/tissue engineering, vaccine and blood products for treatment or prevention of serious diseases, e.g., HIV, cancer, diabetes, heart disease
- Over last 3 calendar years,
  - ~ 290 - 370 sponsor meetings yearly
  - ~ 7000 - 7800 IND/IDE amendments yearly
  - ~ 1650 - 2100 BLA supplements yearly

CBER is meeting its performance goals for PDUFA and MDUFMA

CBER Initiatives: Meeting present needs and planning for the future

- Pandemic influenza and counter terrorism
- Enhance safety
- Bring safe and effective products to patients
- Improve manufacturing and product quality
- Implement management and organizational improvements
- Foster Critical Path initiatives

Pandemic Influenza



Pandemic Influenza

- **Improve preparedness for an influenza pandemic by**
  - **Facilitating rapid development and licensing of new vaccines**
  - **Fostering development of biological therapeutics**
  - **Minimizing impact of pandemic on public health infrastructure and the blood supply**

Meeting the pandemic influenza vaccine challenge: overview and actions

- Developing needed pathways and regulatory processes to speed vaccine availability
- Facilitating vaccine manufacturing and availability
  - Increasing manufacturing diversity and capacity
  - Addressing scientific and related technical needs
  - Enabling both current and evolving technologies
- Assuring safety and public confidence
- Considering pathways to prevent a pandemic
- Global assistance, cooperation, harmonization

CT and Emerging Infections
Not business as Usual

- Apply appropriate regulatory strategies to facilitate rapid product development
- Early and intensive interactions with product sponsors
- Collaborative product reviews, use of multiple product development teams
- Proactive facility inspections
- Build on our successes… learn from every experience (CT, flu season, West Nile virus, and pandemic planning)

CBER CT Efforts

- **Facilitating development of products under IND**
  - **New smallpox vaccines**
  - **New anthrax vaccines**
  - **Anthrax immune globulin**
  - **Botulinum antitoxin**
- **Two VIG products to treat complications of smallpox vaccination approved (2005)**
- **Product availability pathways include IND, EUA, fast track, accelerated approval, priority review, "animal rule"**

Enhance Safety of CBER-Regulated Products

- Implement integrated approaches to improve
  - early detection, analysis, and communication about product safety issues
  - using available technology, including health care data bases

Improve dissemination of health care provider and consumer safety information

- CBER exhibit program (brochures, fliers, presentations, internet communications), including benefit and risk communication information for consumers
- Better utilization of public advisory processes (e.g., FDA Advisory Committees and DHHS Advisory Committee on blood safety)
- Employ high visibility publications and presentations addressed to health care providers

Safety Initiatives: Integrated Product Safety Teams

- Formation of integrated safety teams (e.g., epidemiologists, clinical/product reviewers, compliance/inspectional activities, communications) in all product areas to improve acquisition and utilization of safety information
  - Follow-up on adverse event reports
  - Encompass entire product life cycle: enhance safety through prevention of medical errors, contamination, manufacturing deviations and unsafe practices
  - Active use of health care databases
  - Proactive: set research, policy & outreach agendas
  - Coordinate the center response to emerging safety issues in collaboration with other FDA Centers and HHS agencies
- Tissue safety team established, blood and vaccine safety teams under development

Bring Safe and Effective Products to Patients

- Implement innovative approaches to accelerate product development and streamline regulation to
  - Promote public and individual health through 21st century medicine,
  - Improve preparedness for pandemic influenza and support development of medical products for counter terrorism
  - Enhance responsiveness to emerging threats (in particular, blood and tissue safety)

Getting Safe and Effective Products to Patients: Focus Areas

- Reviewer templates and managed review process enhancements and training
- Strategies to augment review expertise (expert consultants within and outside FDA)
- CBER/CDRH Tissue Engineering cross-center review team
- Critical path activities
- Enhance emergency preparedness

Manufacturing and Quality

- **Enhance risk-based, scientific oversight of manufacturing throughout the life cycle of CBER-regulated products**

Manufacturing and Quality

- Continue efforts to modernize regulations and where possible to harmonize with other regulatory authorities
- Guidance development
- Training and outreach initiatives (e.g., site visits, quality training, workshops)
- Lot release program enhancements
- Risk-based compliance programs
  - Evaluate existing programs
  - Expand to new areas

Management and Leadership Initiatives

- Transform our business practices by strengthening
  - Human capital
  - Leadership
  - Management systems, including IT capabilities

Management Initiatives

- Enhance effective use of staff expertise (ongoing management and leadership training, core competency based reviewer training)
- Gap analysis-based succession planning (recruitment and training)
- Enhance communication strategies (internal)
- Improve IT capabilities to meet current and emerging needs
- Implement quality system principles

CBER Critical Path: Bridge from Discovery to Products for Better Health

Biomedical Discovery

Products Improving Lives and our Nation's Health & Preparedness

- **Unique focus: Research managed to identify solutions to product development challenges: tools and pathways to help cross the bridge from discovery to real products**

Critical Path: Problem Solving CBER Research

- **FDA/ CBER focus: research managed to identify solutions to product development challenges**
  - **Driven by FDA perspectives & data, the "Big Picture"**
  - **Performed by active reviewers on multi-disciplinary teams, help identify issues & set research priorities**
  - **Not NIH or industry research - applied to concrete product issues**
  - **Often cross-cutting: clinical, product, statistical elements**
  - **Collaborative & leveraging: internal and external resources**
  - **Increased transparency and external input through Advisory Committee Office Site Visits**

Critical Path Science Investment Opportunities: Examples

- Develop/make available well characterized cell banks for biologics production – & update guidance
- Characterization of cell therapies and links to standardized clinical/lab outcomes
- New assays, standards, biomarkers, surrogates for biologics safety, efficacy, and quality
- Methods and validation of pathogen inactivation for blood, plasma, tissues and other products
- Multi-pathogen and rapid detection methodologies
- Improving longevity/storage of blood and tissues
- Enhanced clinical trial design/analysis

CBER Collaborative Science Supporting Innovation

- Potency/effectiveness/standards
  - High throughput test to measure immune response to smallpox vaccine and VIG potency
  - International clotting factor, thrombin, adenovirus standards
  - Proteomic monitoring of cancer treatment
  - Surrogate markers/models of efficacy; TB, tularemia, hep C, pneumococcus, IGIV
  - Embryonic stem cell gene expression
- Safety
  - West Nile testing standards and reagents
  - Vaccine/cell safety and adventitious agent tests

Thank you

focus
innovate
succeed

- **We are proud of our staff and our role in public health, biodefense and the development & availability of new products for the 21st century**
- **New technologies need expert, innovative, interactive review, regulation and science, new models, standards, assays – CBER products are important in "Critical Path"**
- ***Together we can build bridges to turn discoveries into products to better lives – safer, better, faster***
- **We see a positive future with exciting products**

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CBER: Innovative Technology Advancing Public Health

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